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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,455	06/18/2001	Michael Houghton	223002010004	1938

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/884,455	HOUGHTON ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed on 31 October 2007 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 October 2007 has been entered. Claims 27-36 were not amended and remain in the application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 27-30 remain rejected for reasons of record under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,585,258. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claims 31-35 remain rejected for reasons of record under the judicially created doctrine of obviousness- type double patenting as being unpatentable over claims 5-9 of U.S. Patent No. 5,585,258 in view of Benson et al., U.S Patent No. 5,258,496. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claim 36 remains rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-5 of U.S. Patent No. 5,597,691. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claims 27 and 30 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent

No. 5,712,145. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claims 31, 32 and 35 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-5 of U.S. Patent No. 5,712,145 in view of Benson et al., U.S Patent No. 5,258,496. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claim 36 remains rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 8 of U.S. Patent No. 5,712,145. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

The following are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Claims 27 and 30 remain provisionally rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 10/409,094, an application for reissue of U.S. Patent No. 5,585,258. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claim 36 remains provisionally rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of copending Application No. 10/409,673, an application for reissue of U.S. Patent No. 5,597,691. Although pages 5 and 5 of the Response of 31 October 2007 indicate that Applicant will file a terminal disclaimer upon indication of allowable subject matter herein, the rejection must be maintained until and unless an effective terminal disclaimer is filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-36 remain rejected for reasons of record under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant's arguments at pages 5-16 of the Response filed 31 October 2007 have been fully considered but are not persuasive. Applicant suggests that the communication mailed 2

May 2007 had not "set out a prima facie case of [a] lack of [adequate] written description" and points out that that the particular appellate decision first cited in the communication mailed 1 July 2004, had not been specifically cited in the more recent communication. Since the decision is particularly pertinent to analysis of the presence or absence of an adequate written description in inventions in the art of biotechnology, it is again noted:

> "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano,* 25 USPQ2d 1601, 1605 (Fed. Cir. 1993).

Indeed, the "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the Inventor had possession at that time of the . . . claimed subject matter", *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983). Applicant also suggests that the USPTO Guidelines for analysis of compliance with the written description requirement cannot supplant application of the law established by appellate decisions. Yet the Guidelines do not set aside factual analysis as a basis for determining whether the statutory requirement is met. They instead require a factual analysis of the presence in, or absence from, the specification of an adequate written description of the **claimed** subject matter, stating that an applicant may comply with the written description requirement by showing that an "invention is **complete** by disclosure of **sufficiently detailed, relevant identifying characteristics** . . . i.e., complete or partial structure, other physical and/or chemical properties, function characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." **Guidelines**, 66 Fed. Reg. 1099 at 1106 (5 January 2001) (emphasis supplied). The Federal Circuit adopted the USPTO's standard for determining compliance with the written description requirement in a decision in the biotechnological arts, *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through (i) a sufficient description of a representative number of species by actual reduction to practice, (ii) a reduction to drawings, (iii) a disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, (iv) by functional characteristics coupled with a known or disclosed correlation between function and structure, or (v) by a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. Thus, one must describe a sufficient variety of species to reflect the variation within the genus where there is substantial variation within the

genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that an applicant had possession of the necessary common attributes or features of elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus embracing widely variant species cannot be achieved by disclosing one species within the genus.

Applicant asserts at page 7 of the Response that the specification discloses an HCV NS3 domain protease "that corresponds to the HCV NS3 serine protease activity" and, alternatively, "corresponds to the HCV NS/23 serine protease activity". The claims are drawn to an isolated HCV polypeptide that "comprises an HCV NS3 domain protease or an active HCV NS3 domain protease truncation analog" wherein the truncation analog has a series of successively smaller "partial internal amino acid sequence[s]" – SEQ IDs NOs:63, 64, or 65 – fusion polypeptides that comprise such "HCV NS3 domain protease[s]" or "active HCV NS3 domain protease truncation analog[s]", and a method for assaying inhibitory compounds by contacting any of these generic products with candidate inhibitors and measuring inhibition of a generic proteolytic activity. The products claimed are members of a broad genus because the most extensive structure actually required for any product is the 202-amino acid sequence of SEQ ID NO:65 and the amino acid sequence of the rest of the NS3 domain protease can vary to any conceivable extent in regions amino-proximal to, and carboxyl-proximal to, the boundaries of SEQ ID NO:65. SEQ IDS NOs:63 and 64 are but a separate undecapeptide and nonapeptide within SEQ ID NO:65 thus claims 27-29 and 31-34 are drawn to very broad genera of products and claim 36 to a method of use of members of the broad genus of products of, at least, claims 30 and 35, as well as members of the far broader genera of products of claims 27-29 and 31-34 that admit alteration of the majority of positions in the 202-amino acid sequence of SEQ ID NO:65. See page 9, line 7, through page 11, line 9, of the specification. The claims require no particular activity but, if Applicant sought to amend the claims to indicate anything other than a generic "protease" or "serine protease" activity, the specification suggests, at pages 19-21, that peptides comprising at least two consecutive arginines, three particular peptides set forth in SEQ IDs NOs:36, 88, and 89, and even the HCV polyprotein, are all potential substrates.

Applicant does not argue that the specification discloses a number of species adequate to demonstrate that Applicant was indeed in possession of any of the broad genera indicated in the claims. Applicant argues instead that the specification discloses at least one "NS3 domain" having "a NS3 serine protease activity" and points to the "Office Action at page 6" for agreement with this proposition. The discussion at pages 6-7 of the communication mailed 2 May 2007 instead concerns Declarations under 37 CFR 1.132 submitted 12 February 2007 and concludes that they provide no corroboration that the events reported in Example 5 of the specification

reflect a proteolytic activity by any of the fusion polypeptides disclosed in the specification. The language quoted by Applicant at page 8 of the Response is instead a quote abstracted from the specification to illustrate an argument made at page 6 of the communication mailed 12 January 2006, rather than a concession. Applicant recapitulates the arguments made in the Response filed 12 February 2007 but argues limitations not found in the claims, which remain unamended, and Applicant's arguments premised on a HCV NS/23 serine protease activity cannot be a basis for amending the claims where there is no disclosure or suggestion of this activity in the specification. As noted at page 7 of the communication mailed 2 May 2007 with respect to the events reported in Example 5 of the specification, "What a skilled artisan would understand from the disclosure of the specification is that the p300, p500, and p600 fusion proteins were cleaved, and that the p190 fusion protein was not cleaved, but would find no evidence therein as to the nature of the protease producing the cleavage nor even evidence of the site in the fusion protein where the cleavage occurred other than the size of the fragment on the SDS gel which fails to agree with what one would expect from a cleavage at the NS2/3 cleavage site as discussed above. Instead, the only available evidence as to what protease produced the cleavage, i.e., the size of the cleavage fragment produced, leads away from a conclusion that the cleavage was produced by a HCV NS2/3 protease." The rejection of record is maintained.

Claims 27-36 remain rejected for reasons of record 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for preparing a protein of the claimed compositions and assay having HCV-specific protease activity, including the P600, P500, P300 or P190 proteins and generic versions or active truncation analogs thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

Applicant's arguments at pages 16-20 of the Response filed 31 October 2007 have been fully considered but are not persuasive. Applicant suggests at page 21 of the Response that the specification discloses an adequate substrate, "in the form of [the] HCV polyprotein" with which experimentation might be conducted, and that its use "for testing NS3 serine protease activity in *trans*", might require no undue experimentation on the part of the artisan to make HCV NS3 domain proteases commensurate in scope with the recitations of the claims rejected herein. With regard to what may constitute "undue experimentation", the CCPA, the precursor of the Court of Appeals for the Federal Circuit, determined that a **reasonable correlation** must exist between the **scope asserted** in the claimed subject matter and **the scope of the guidance** the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (emphasis supplied). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Yet the teaching of the specification that the amino acid sequence of SEQ ID NO:65, the most particular

embodiment described by claims 30 and 35, cannot be combined with the state of the art at the time the specification was filed to permit the preparation of a claimed protease, or the practice of a claimed assay with a such a protease, by an artisan at that time without undue experimentation. This is because, while SEQ ID NO:65 includes all residues necessary for NS3 domain serine protease cleavage at the NS5A/5B junction, it includes no amino acid sequence region that permits cleavage at the NS2/3 junction by a NS2/3 metalloprotease or cleavage at any of the NS3/4A, NS4A/4B or NS4B/5A junctions by a NS3 serine protease. Indeed, the only substrates that the specification proposes are not substrates of the NS3 domain serine protease of SEQ ID NO:65. These are teachings found at pages 19-21 of the specification discussed in the preceding rejection and discussed more fully at pages 8 and 9 of the communication mailed 2 May 2007. Applicant argues at page 22 of the Response that the teaching of the amino acid sequence of SEQ ID NO:65 and the availability of an HCV polyprotein substrate would guide the artisan to prepare products that might populate the genera of proteases embraced by claims 27-35 rejected herein, and practice an assay of claim 36 with such generic products but there is no guidance in the specification as to what more might be required beyond the amino acid sequence of SEQ ID NO:65 to locate the sequence of NS4A cofactor, a cofactor is not present in SEQ ID NO:65 which was discovered in the art well after the date for the disclosure of the specification herein, that could bring about cleavage of the native polyprotein. See Failla et al., Ref 433, and Lin et al., Ref 601. Because the scope of guidance provided by the specification does not indicate the direction the artisan might take to begin the next, necessary, process of experimentation, the rejection of record is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-36 remain rejected for reasons of record under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant' arguments at pages 22-24 of the Response filed 31 October 2007 have been fully considered but are not persuasive. Applicant suggests at page 23 of the Response the recitation of a "purified proteolytic HCV polypeptide" permits the artisan and the public to understand that a "NS3 domain hepatitis C virus [proteases or] protease truncation analog[s]" must have some protease activity defining the boundaries of the claimed subject matter. Yet claims 27, 31, and 36 recite no particular functional description of the protease activity of such proteases, and the range of complexity of structures of truncation analogs that the artisan and the public can identify in claims 28-30 and 31-35 – an order of magnitude between the small, unconnected, and dissimilar peptides of claims 28, 29, 33, and 34 and the 202-amino acid

sequence of SEQ ID NO:65 of claims 30 and 35 – provides no basis for distinguishing the size or structure of the polypeptides of 27 and 31 needed for an assay of 36 which may well be an HCV polyprotein since it is yet another order of magnitude larger. The premise of the argument thus equally identifies an HCV polyprotein and all available truncation analogs and the absence of a disclosure in the specification of a specific amino acid sequence possessing a particular protease activity that might be a basis for amending the claims is clear indication that the claims describe no definite, initial, structure that allows the artisan and the public to ascertain a reference point from which they might begin to measure the metes and bounds of the claims. It is agreed that "functional language", if it is itself definite, "does not in and of itself, render a claim improper" but claims 27-36 rejected herein lack both a particular function and a basis for measuring what might provide some function. The rejection of record is therefore maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner, Art Unit 1656

William W. Moore
9 November 2007